1 ANSWER 2 OF 49 MEDLINE
AN 2001522473 MEDLINE
DN 21453755 PubMed ID: 11567612
TI APP processing and **synaptic** plasticity in **presenilin**-1 conditional knockout mice.
AU Yu H; Saura C A; Choi S Y; Sun L D; Yang X; Handler M; Kawarabayashi T; Younkin L; Fedeles B; Wilson M A; Younkin S; Kandel E R; Kirkwood A; Shen J
CS Center for Neurologic Diseases, Brigham and Women's Hospital, Boston, MA 02115, USA.
SO NEURON, (2001 Sep 13) 31 (5) 713-26.
Journal code: AN8; 8809320. ISSN: 0896-6273.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200110
ED Entered STN: 20010925
Last Updated on STN: 20011022
Entered Medline: 20011018
AB We have developed a **presenilin**-1 (PS1) conditional knockout mouse (cKO), in which PS1 inactivation is restricted to the postnatal forebrain. The PS1 cKO mouse is viable and exhibits no gross abnormalities. The carboxy-terminal fragments of the amyloid precursor protein differentially accumulate in the cerebral cortex of cKO mice, while generation of beta-amyloid peptides is reduced. Expression of Notch downstream effector genes, Hes1, Hes5, and Dll1, is unaffected in the cKO cortex. Although basal **synaptic** transmission, long-term potentiation, and long-term depression at hippocampal area CA1 **synapses** are normal, the PS1 cKO mice exhibit subtle but significant deficits in long-term spatial memory. These results demonstrate that inactivation of PS1 function in the adult cerebral cortex leads to reduced Abeta generation and subtle cognitive deficits without affecting expression of Notch downstream genes.

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DN 20138533 PubMed ID: 10671322
TI Enhanced synaptic potentiation in transgenic mice expressing presenilin 1 familial **Alzheimer**'s disease mutation is normalized with a benzodiazepine.
AU Zaman S H; Parent A; Laskey A; Lee M K; Borchelt D R; Sisodia S S; Malinow R
CS Cold Spring Harbor Laboratory, Cold Spring Harbor, New York 11724-0100, USA.
NC 1PO1AG14248 (NIA)
SO NEUROBIOLOGY OF DISEASE, (2000 Feb) 7 (1) 54-63.
Journal code: CUN; 9500169. ISSN: 0969-9961.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200003
ED Entered STN: 20000407
Last Updated on STN: 20000407
Entered Medline: 20000329
AB Mutations in presenilin 1 (PS1) are the most common causes of familial **Alzheimer**'s disease (FAD). We examined synaptic physiology in hippocampal brain slices of transgenic mice expressing the FAD-linked PS1 deletion of exon 9 variant. Basal excitatory transmission and paired-pulse facilitation in PS1 mutant mice were unchanged. Short- and **long-term potentiation** of excitatory transmission following high-frequency stimulation were greater in transgenic mice expressing mutant PS1. Mutants had enhanced synaptic **inhibition**, which may be a compensatory change offsetting an abnormally sensitized plasticity of excitatory transmission. Increasing inhibitory transmission in mutant animals even more with a benzodiazepine reverted synaptic potentiation to the levels of controls. These results support the potential use of benzodiazepines in the treatment of familial **Alzheimer**'s d

ED Entered STN: 19990326
Last Updated on STN: 19990326
Entered Medline: 19990318

AB Alzheimer's disease is characterized by amyloid beta-peptide deposition, **synapse** loss, and neuronal death, which are correlated with cognitive impairments. Mutations in the **presenilin**-1 gene on chromosome 14 are causally linked to many cases of early-onset inherited Alzheimer's disease. We report that **synaptosomes** prepared from transgenic mice harboring **presenilin**-1 mutations exhibit enhanced elevations of cytoplasmic calcium levels following exposure to depolarizing agents, amyloid beta-peptide, and a mitochondrial toxin compared with **synaptosomes** from nontransgenic mice and mice overexpressing wild-type **presenilin**-1. Mitochondrial dysfunction and caspase activation following exposures to amyloid beta-peptide and metabolic insults were exacerbated in **synaptosomes** from **presenilin**-1 mutant mice. Agents that buffer cytoplasmic calcium or that prevent calcium release from the endoplasmic reticulum protected **synaptosomes** against the adverse effect of **presenilin**-1 mutations on mitochondrial function. Abnormal **synaptic** calcium homeostasis and mitochondrial dysfunction may contribute to the pathogenic mechanism of **presenilin**-1 mutations.

L1 ANSWER 38 OF 49 MEDLINE
AN 1998245169 MEDLINE
DN 98245169 PubMed ID: 9576681
TI The Alzheimer's plaques, tangles and memory deficits may have a common origin; part I; a calcium deficit hypothesis.
AU Chen M
CS Department of Pharmacology and Therapeutics, University of South Florida, College of Medicine, Tampa, Florida, USA.. michen@com1.med.usf.edu
SO FRONTIERS IN BIOSCIENCE, (1998 May 11) 3 a27-31. Ref: 45
Journal code: CUE; 9702166. ISSN: 1093-4715.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 199808
ED Entered STN: 19980820
Last Updated on STN: 20000303
Entered Medline: 19980813

AB Review of the literature reveals that several biochemical events implicated in the pathology of Alzheimer's disease (AD) are calcium dependent processes. These processes include normal processing of beta-amyloid precursor protein, dephosphorylation and degradation of tau, neurotransmitter release and memory formation. Since all of these processes appear to be inactivated during progression of AD, we propose that a "deficit" of intracellular calcium levels may occur in the early phase of the disease. We also propose several experiments to test this hypothesis. The hypothesis predicts that **presenilins** most likely act as calcium channels in vivo and that their gene mutations may cause the disease by diminishing the Ca2+ channeling function.

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